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EVALUATION OF THE ACUTE TOXICITY OF SILAHYDROCARBON

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TECHNICAL REVIEW AND APPROVAL

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The experiments reported herein were conducted according to the "Guide for the Care and Use of Laboratory Animals," Institute of Laboratory Animal Resources, National Research Council.

This report has been reviewed by the Office of Public Affairs (PA) and is releasable to the National Technical Information Service (NTIS). At NTIS, it will be available to the general public, including foreign nations.

This technical report has been reviewed and is approved for publication.

FOR THE COMMANDER

MICHAEL B. BALLINGER, Lt Col, USAF, BSC
Chief, Toxic Hazards Division
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Silahydrocarbon (SHC) is a base stock for a candidate high-temperature hydraulic fluid. A complete battery of acute toxicity tests were performed to determine the potential health hazard of the fluid. A single neat dose of 0.1 mL SHC into NZW rabbit eyes resulted in slight conjuctivae irritation one hour after treatment in all unflushed eyes and one of three flushed eyes. Conjunctival irritation persisted through 24-hours but was dissipated by 48 hours. Rinsing the eyes after treatment was of questionable benefit. Single treatment of 0.5 mL neat SHC to rabbit skin produced negative results for all but a single animal, which had very slight erythema at the test site 48 hours after treatment. Guinea pigs failed to elicit a sensitization response following repeated application of SHC. A single oral dose of 5g SHC/kg of animal body weight to five male and female F-344 rats, and a single dermal application of 2g SHC/kg body weight applied to five male and five female NZW rabbits resulted in no deaths. No signs of toxic stress were observed, and all animals gained weight during the 14-day post-treatment observation periods. Inhalation exposure to SHC was performed by exposing five male and five female F-344 rats to a 4.8 mg/L near limit concentration of aerosolized SHC for four hours. All surviving rats gained weight during the 14-day post-treatment observation period

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PREFACE

This is one of a series of technical reports describing results of the experimental laboratory programs conducted at the Toxic Hazards Research Unit, NSI Technology Services Corporation-Environmental Sciences. This document serves as a final report on the in-life toxicity of silahydrocarbon. The research described in this report began in January 1989 and was completed in June 1989 under U.S. Air Force Contract No. F33615-85-C-0532. Melvin E. Andersen, Ph.D., served as Contract Technical Monitor for the U.S. Air Force, Harry G. Armstrong Aerospace Medical Research Laboratory.

The animals used in this study were handled in accordance with the principles stated in the *Guide for the Care and Use of Laboratory Animals*, prepared by the Committee on Care and Use of Laboratory Animals of the Institute of Laboratory Animal Resources, National Research Council, Department of Health and Human Services, National Institute of Health Publication #86-23, 1985, and the Animal Welfare Act of 1966, as amended.

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ABBREVIATIONS

CFM	Cubic feet per minute
cm	Centimeter
F-344	Fischer 344 (rats)
g	Gram
h	Hour
kg	Kilogram
L	Liter
µm	Micrometer
mg	Milligram
min	Minute
mL	Milliliter
mm	Millimeter
NZW	New Zealand White (rabbits)
psi	Pounds per square inch
sec	Second
SEM	Standard error mean
SHC	Silahydrocarbon

SECTION 1

INTRODUCTION

Silahydrocarbon (SHC) is a base stock for a candidate high-temperature hydraulic fluid developed and made by the Air Force Materials Laboratory (AFWAL/MLBT). The Materials Laboratory is presently conducting compatibility tests of SHC with high-temperature hydraulic seals and advanced structural materials. At present, the Materials Lab has completed a 500-h low-temperature (275°C) pump test. Since Air Force personnel are already working with SHC, and SHC shows promise as a base stock for hydraulic fluids, potential acute toxicity hazards must be addressed.

The most significant exposure routes for hydraulic fluids are expected to be dermal, due to spills or leaks, and aerosol inhalation from pressurized system leaks. This study addressed these potential routes of exposure and included experiments designed to assess eye and skin irritation, skin sensitization, single dose oral and dermal toxicity, and aerosol inhalation toxicity. Species and sex of animals selected for these acute toxicity tests were in conformance with the requirements of the Environmental Protection Agency. Existing alternative methods to animal testing were inadequate for use in this study.

SECTION 2

MATERIALS

TEST AGENT

The test material used in this study was supplied by the Air Force. In general, SHCs are defined as compounds represented by the structure SiR4. The sample tested was identified as follows:

Silahydrocarbon MLO 86-348

Pertinent physical characteristics:

Flash Point (°C):	221
Fire Point (°C):	237
Density @ 25°C:	0.8145
Density @ 100°C:	0.7671

Mol Wt (principal "R" components):	
methyltrioctyl	382.1
methyldioctyldecyl	410.1
methyloctyldidecyl	438.1
Viscosity (cSt) at:	
-54°C (-65°F)	2168
-40°C (-40°F)	548
40°C (104 F)	9.20
100°C (212°F)	2.71

ANIMALS

Male Fischer 344 (F-344) rats weighing between 100 and 125 g and female F-344 rats weighing between 75 and 100 g were purchased from Charles River Breeding Labs, Kingston, NY. Male Hartley guinea pigs weighing between 200 and 250 g were purchased from Murphy Breeding Labs, Plainfield, IN. Male and female New Zealand White (NZW) rabbits weighing between 2 and 3 kg were purchased from Clerco Research Farms, Cincinnati, OH. All animals were subjected to a two-week quarantine period. Rats were group housed (three per cage) in clear plastic cages with wood chip bedding. The guinea pigs and rabbits were housed individually, the guinea pigs in plastic cages with wood chip bedding, and the rabbits in wire-bottom, stainless-steel cages. Water and feed (Purina Rabbit Chow #5320, Purina Formulab #5008 for rats, and Purina Formulab #5025 for guinea pigs) were available *ad libitum*, except during the inhalation exposure period and for 16 h prior to oral dosing. Animal room temperatures were maintained at 21° to 25°C and the light/dark cycle was set at 12-h intervals.

SECTION 3

EXPERIMENTAL APPROACH

EYE IRRITATION

Nine NZW female rabbits, weighing between 2 and 3 kg, were examined with fluorescein stain prior to use to ensure absence of lesions or injury. A topical anesthetic (Ophthetic, Allergan Inc., Irvine, CA; Proparacaine HCl 0.5%) was instilled in the eyes of all rabbits, treated and control, approximately 2 min prior to application of the test material. One tenth of a mL of the test material was applied to one eye of each of the nine rabbits. The opposite eye was left untreated and served as the control. The treated eye of three rabbits was flushed with lukewarm deionized water for 1 min starting 30 sec after instillation. The eyes of the remaining six rabbits were not flushed. Examinations for gross signs of eye irritation were made at 1, 24, 48, and 72 h following treatment. Irritation was

scored according to the method of Draize et al. (1944, **Appendix A**), in which the total score for the eye was the sum of all scores obtained for the cornea, iris, and conjunctiva.

SKIN IRRITATION

Six NZW female rabbits were clipped on the back and sides 24 h prior to dosing to allow for recovery of the skin from any abrasion resulting from the clipping. The test agent (0.5 mL) was applied to a designated patch area and was covered by a 3 cm square of surgical gauze two single layers thick. Strips of surgical adhesive tape held the gauze patch in place and the entire shaved area was covered with dental dam and secured with Vetrap (3M Corp., Minneapolis, MN) and adhesive tape. The patches remained in place for 4 h, then all wrappings were removed and the residual test agent wiped from the skin. Test areas were evaluated for irritation using the Draize Table (Draize et al. 1959, **Appendix B**) as a reference standard at 4, 24, 48, and 72 h. Total scores of the four observations for all rabbits were divided by 24 to yield a primary irritation rating which was interpreted using the National Institute for Occupational Safety and Health skin test rating (**Appendix C**).

SENSITIZATION

Prior to the start of the study, ten male guinea pigs were treated on the clipped left flank with 0.1 mL of the undiluted test material to determine the baseline irritation response. The site of the sensitization test was an area just behind the shoulder girdle. This site was clipped with an Oster® animal clipper and depilated with a commercial depilatory (Surgex Hair Remover Cream, Sparta Instrument Corp., Hayward, CA) 4 h prior to treatment. A Vetrap frame with a 1.5 x 1.5 cm opening was affixed to the guinea pig at the site of the depilated area. One-tenth of a mL of the test material was topically applied to the test area and covered with gauze, dental dam, and adhesive tape. This was done on Mondays, Wednesdays, and Fridays until a total of four sensitizing treatments were applied and evaluated. At the time of the third sensitizing treatment, 0.2 mL of a 50% aqueous dilution of Freund's adjuvant (Bacto Adjuvant Complete, Freund, Difco Laboratories, Detroit, MI) per animal was injected intradermally using two or three sites next to the test site. Following the fourth sensitizing treatment, the animals were rested for two weeks. Both flanks were then clipped and challenged on one flank with 0.1 mL of the test material. The challenge application was not occluded. The skin response at these sites was recorded at 4, 12, 24, and 48 h after application (scoring method in **Appendix D**). Any animal eliciting a score of two or more at the test solution challenge site at the 48 h scoring interval was rated a positive responder. The percentage of animals responding was the important factor in determining sensitization potential. **Appendix E** was used to classify the test materials as to sensitization potential.

ORAL TOXICITY

Five male and five female F-344 rats were fasted 16 h prior to the administration of the oral dose. Each rat was weighed prior to oral gavage dosing and 5 g/kg of neat compound was administered. Surviving rats were weighed at 1, 2, 4, 7, 10, and 14 days postexposure and signs of toxicity recorded. On the 14th day postexposure, rats were sacrificed and gross pathology was performed.

DERMAL TOXICITY

Twenty-four hours prior to dosing, the back and sides of five male and five female NZW rabbits were clipped. The undiluted dose of 2 g/kg was applied to the back of the rabbits and spread evenly to both sides. The dose was kept in place by applying an eight-ply gauze patch over the liquid. A clear plastic wrap was then applied over the entire midsection and was held in place with Vetrap and elastoplast tape. The dose was kept in contact with the rabbit skin for 24 h. The tape, plastic wrap, and gauze were then removed and the residual test material was wiped from the animal. Animal body weights were recorded on days 1, 2, 4, 7, 10, and 14 post-treatment. Signs of toxicity and mortality were monitored and gross pathology was performed at the termination of the study.

INHALATION EXPOSURE

The aerosol generation system consisted of a 250 mL, round-bottom flask containing a 6-jet Collison (BGI, Inc., Waltham, MA) compressed air nebulizer operated at a pressure of 50 psi (**Figure 1**). The 690-L chamber was operated at a mean flow rate of 0.79 CFM providing two chamber volumes of air per hour. Exposure concentration was controlled by adjusting the chamber air flow.

Eight Metricel (Gelman Sciences, Inc., Ann Arbor, MI) membrane filter samples of chamber atmospheres were taken during the course of the 4-h exposure. These were gravimetrically analyzed for mass concentration by dividing the weight change by the volume sampled. Aerosol particle size distributions were measured with a Lovelace Multijet Impactor (Intox Products, Albuquerque, NM). Two 30-sec samples were taken during the exposure. A Varian 3700 (Varian Associates, Palo Alto, CA) gas chromatograph equipped with a 3-m, 0.25-mm fused silica SE-30 capillary column and flame ionization detector was utilized to obtain profiles of the SHC as received, as aerosolized, and as a residue from the nebulizer system.

Five male and five female F-344 rats were placed in a 690-L chamber and exposed for 4 h to a target 5 mg/L (limit test) concentration of aerosolized test material. Records were maintained for body weights (day 0, 7, 10, and 14 postexposure), signs of toxicity, and mortality. At sacrifice, gross pathology was performed and lungs were removed for histopathologic evaluation.

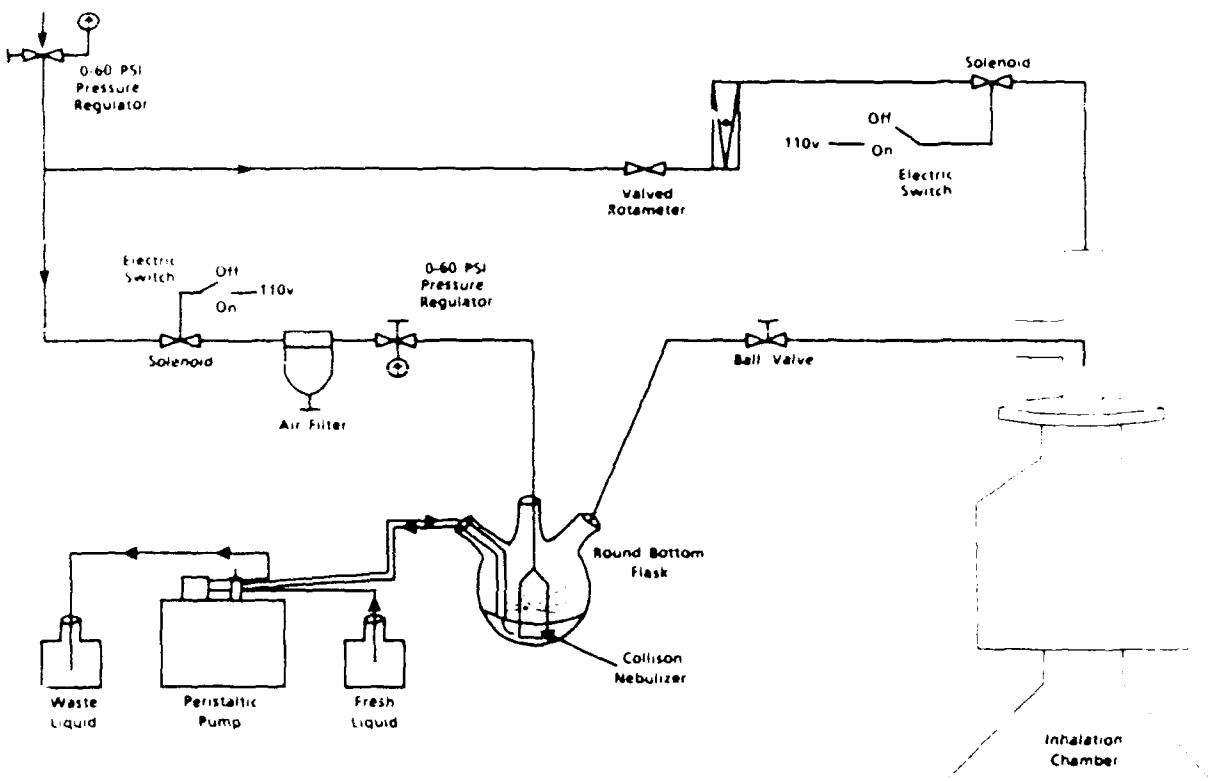

Figure 1. Test Atmosphere Generation System for Silahydrocarbon.

STATISTICAL ANALYSIS

Mean body weights of the inhalation rats were compared using the Multivariate Analysis of Covariance for Repeated Measures Test (Barcikowski, 1983). A probability of 0.05 or less inferred a significant change from controls.

SECTION 4

RESULTS

EYE IRRITATION

The instillation of 0.1 mL of SHC in rabbit eyes produced no corneal opacity or congestion, swelling, or discharge of the iris when test animals were observed at 1, 24, 48, or 72 h postinstillation. However, slight irritation of the conjunctivae was noted in all unflushed eyes and one of the three flushed eyes 1 h after treatment. Conjunctival irritation persisted through the 24-h readings but had dissipated by 48 h (**Table 1**).

SKIN IRRITATION

Six rabbits were treated dermally with 0.5 mL of SHC. No erythema, edema, or necrosis was observed in any of the rabbits upon examination immediately following 4-h dermal contact with the test agent (**Table 2**). Subsequent observations at 24, 48, and 72 h were also negative, except for a single animal that had very slight erythema at the test site 48 h after treatment.

SENSITIZATION

No test animals exhibited erythema or edema following the baseline response treatment of 0.1 mL test material to the shaved flank. Following 10 days of sensitization dosing and two weeks of rest, the test animals were challenged with 0.1 mL of the test material. The SHC produced no erythema or edema at 24 or 48 h after this challenge treatment (**Table 3**).

ORAL TOXICITY

Five male and five female rats were orally dosed with 5 g of SHC/kg body weight. No deaths resulted from the oral administration of the test agent and no signs of toxicity were observed. All rats gained weight during the 14-day observation period (**Table 4**).

DERMAL TOXICITY

Five male and five female rabbits were treated with 2 g of SHC/kg body weight. No deaths occurred from the 24-h contact with the test agent and no signs of toxicity were observed. All rabbits gained weight during the 14-day observation period (Table 5).

TABLE 1. PRIMARY EYE IRRITATION SCORES FOLLOWING INSTILLATION OF SILAHYDROCARBON

Rabbit No.	Eyes Washed	Examination Time (Hours Post-treatment)			
		1	24	48	72
X96	No	2	0	0	0
Y00	No	2	0	0	0
Y02	No	2	2	0	0
Y04	No	2	0	0	0
Y06	No	2	0	0	0
Y08	No	2	2	0	0
Y10	Yes	0	0	0	0
Y12	Yes	2	2	0	0
Y14	Yes	0	2	0	0

TABLE 2. PRIMARY SKIN IRRITATION SCORES FOLLOWING DERMAL CONTACT WITH SILAHYDROCARBON

Rabbit No.	Examination Time (Hours Post-treatment)			
	4	24	48	72
X94	0	0	0	0
Y04	0	0	0	0
Y08	0	0	0	0
Y10	0	0	0	0
Y12	0	0	0	0
Y14	0	0	0	0

TABLE 3. SKIN SENSITIZATION TEST SCORES FOR CHALLENGE APPLICATION OF SILAHYDROCARBON

Guinea Pig No.	Erythema / Edema	
	24 h Post-treatment	48 h Post-treatmet
0110005	0/0	0/0
0110006	0/0	0/0
0110007	0/0	0/0
0110008	0/0	0/0
0110009	0/0	0/0
0110010	0/0	0/0
0110011	0/0	0/0
0110012	0/0	0/0
0110014	0/0	0/0
0110015	0/0	0/0
	POSITIVE RESPONDERS = 0%	
	CLASSIFICATION = Non-Responder	

TABLE 4. BODY WEIGHTS (g) OF MALE AND FEMALE RATS AFTER GAVAGE WITH 5 g SILAHYDROCARBON/kg

Sex	Rat No.	Days Post-treatment						
		0	1	2	4	7	10	14
Male	01110001	199.6	215.2	214.4	220.9	233.8	238.5	247.8
Male	01110002	186.5	195.4	198.2	205.0	216.5	218.0	226.3
Male	01110004	189.7	206.4	204.4	208.9	219.1	224.9	235.6
Male	01110005	198.5	213.5	212.9	220.2	231.2	238.8	244.4
Male	01110006	198.0	212.0	211.7	217.5	228.0	229.5	237.3
Male	**mean**	**194.5**	**208.5**	**208.3**	**214.5**	**225.7**	**229.9**	**238.3**
	(± S.E.M.)	**(2.7)**	**(3.6)**	**(3.1)**	**(3.2)**	**(3.4)**	**(4.0)**	**(3.7)**
Female	01110007	114.7	129.0	127.2	132.7	140.6	141.4	146.0
Female	01110008	122.3	135.3	132.4	137.3	143.5	143.2	148.3
Female	01110010	130.2	141.1	139.5	146.0	149.7	151.6	154.1
Female	01110011	115.4	126.0	124.4	128.8	134.8	139.1	143.4
Female	01110012	138.9	149.5	150.3	154.5	159.6	159.3	164.4
Female	**mean**	**124.3**	**136.2**	**134.8**	**139.9**	**145.6**	**146.9**	**151.2**
	(± S.E.M.)	**(4.6)**	**(4.2)**	**(4.7)**	**(4.6)**	**(4.2)**	**(3.7)**	**(3.7)**

TABLE 5. BODY WEIGHTS (g) OF MALE AND FEMALE RABBITS AFTER 24 h DERMAL EXPOSURE TO 2 g SILAHYDROCARBON/kg

Sex	Rabbit No.	Days Post-treatment					
		0	1	2	4	10	14
Male	Y16	2.98	2.79	2.85	3.00	3.20	3.30
Male	Y20	2.78	2.68	2.72	2.89	3.09	3.12
Male	Y22	2.77	2.55	2.70	2.80	3.10	3.21
Male	Y24	2.72	2.58	2.60	2.80	3.02	3.02
Male	Y26	2.99	2.75	2.82	3.01	3.25	3.30
Male	**mean**	**2.85**	**2.67**	**2.74**	**2.90**	**3.13**	**3.19**
	(± S.E.M.)	**(0.06)**	**(0.05)**	**(0.04)**	**(0.05)**	**(0.04)**	**(0.05)**
Female	Y95	2.60	2.32	2.50	2.65	2.84	2.90
Female	Y97	2.98	2.84	2.90	3.02	3.10	3.22
Female	Y99	2.73	2.59	2.61	2.73	2.93	3.20
Female	Z03	2.85	2.62	2.72	2.87	3.15	3.20
Female	Z05	3.00	2.79	2.82	3.09	3.33	3.40
Female	**mean**	**2.83**	**2.63**	**2.71**	**2.87**	**3.07**	**3.18**
	(± S.E.M.)	**(0.08)**	**(0.09)**	**(0.07)**	**(0.08)**	**(0.09)**	**(0.08)**

INHALATION TOXICITY

Eight filter samples were obtained from the chamber during the 4-h exposure. The mean time-weighted chamber concentration was 4.81 mg/L. Mass median aerosol diameter of the sampled test material was 1.58 µm with a standard geometric mean of 1.93. Gas chromatographic analysis of filtered chamber air revealed no SHC in the vapor phase.

Gas chromatographic comparison was made of samples of SHC from filter extracts, impactor plate extract, and aerosol generator waste, as well as whole chamber atmosphere samples. No difference was observed in the chromatographs of four major samples (**Table 6**). No peaks were observed from a chamber vapor atmosphere sample.

All male rats survived a 4-h inhalation exposure to 4.8 mg SHC/L; however, one of five female rats died within 48 h postexposure. During exposure the test animals demonstrated signs of eye and upper respiratory irritation. All surviving rats gained weight during the 14-day observation period (**Table 7**). There was no statistical difference in body weight gain between the treatment groups and their corresponding control groups.

Gross observations at sacrifice failed to reveal any treatment-related lesions and lungs harvested for microscopic examination were unremarkable. Microscopic findings in the lungs of the rat that died included marked, diffuse congestion and edema

TABLE 6. COMPARISON OF GAS CHROMATOGRAPH PEAK AREAS (%) OF SILAHYDROCARBON SAMPLES[a]

Peak Retention Time (mins)	Peak Areas								
	Stock Sample			Generator Waste		Impactor		Filter	
10.9	35.9	36.3	35.7	35.2	35.8	36.4	34.3	35.4	36.0
13.7	45.5	45.7	46.0	46.4	45.9	45.3	47.1	46.1	45.8
16.4	14.0	13.7	13.7	13.9	13.9	14.1	14.1	14.0	13.6
19.8	1.9	1.8	1.9	2.0	1.9	1.8	1.8	1.8	1.8
22.5	2.7	2.6	2.6	2.5	2.5	2.4	2.6	2.6	2.7

[a] Three samples of stock material, two samples each from generator, impactor, and filter

TABLE 7. BODY WEIGHTS (g) OF MALE AND FEMALE RATS AFTER 4-h INHALATION EXPOSURE TO 4.8 mg SILAHYDROCARBON/L

Animal No.	Day 0	Day 7	Day 10	Day 14
CONTROLS				
Males				
0111152	207.0	225.3	226.0	241.4
0111156	203.9	223.1	224.7	241.2
0111157	211.9	227.7	230.2	247.9
0111158	204.0	220.7	224.4	241.4
0111159	209.3	230.0	234.1	251.2
Mean	**207.2**	**225.4**	**227.9**	**244.6**
(± S.E.M.)	**(1.5)**	**(1.6)**	**(1.9)**	**(2.1)**
Females				
0111312	141.1	148.5	147.9	156.7
0111316	137.6	146.2	146.5	155.5
0111318	142.8	153.6	154.6	164.4
0111320	134.1	140.0	140.9	149.1
0111321	143.3	151.7	151.1	162.0
Mean	**139.8**	**148.0**	**148.2**	**157.5**
(± S.E.M.)	**(1.7)**	**(2.4)**	**(2.3)**	**(2.7)**
TREATED				
Males				
0111149	201.5	218.5	223.1	241.0
0111151	196.7	217.6	220.6	234.4
0111154	215.9	227.7	233.6	254.0
0111155	218.3	237.9	235.2	255.3
0111163	198.8	211.6	216.9	230.8
Mean	**206.2**	**222.7**	**225.9**	**243.1**
(± S.E.M.)	**(4.5)**	**(4.6)**	**(3.6)**	**(5.0)**
Females				
0111310	138.8	140.3	140.0	150.6
0111311	143.3	143.2	142.6	154.0
0111313	139.7	---	---	---
0111315	140.6	143.4	146.0	157.8
0111317	136.4	141.9	143.7	156.8
Mean	**139.8**	**142.2**	**143.1**	**154.8**
(± S.E.M.)	**(1.1)**	**(0.7)**	**(1.2)**	**(1.6)**

SECTION 5

DISCUSSION

In the oral and dermal toxicity studies, no deaths or toxic signs were observed in any of the animals and body weight gains during the subsequent 14-day observation period appeared to be unaffected by treatment. SHC exhibited a mild irritating effect to the conjunctival tissue of rabbit eyes. Rinsing the eyes after treatment was of questionable benefit. Remarkable irritating effects were not observed as a result of exposure to intact skin of rabbits nor did the repeat application elicit a sensitization reaction in guinea pigs.

Inhalation of SHC at near the limit concentration produced irritation in all rats and death in one of ten rats. Although one animal died spontaneously within 48 h after exposure to 4.8 mg SHC/m^3 and had histiologic evidence of pulmonary edema, all other animals in the same exposure chamber survived until the end of the 14-day observation period. The absence of any residual evidence of lung injury in the survivors suggests that most animals would experience no prolonged effects as a result of exposure to 4.8 mg/m^3. Physically, the 4.8 mg/m^3 aerosol had the appearance of a dense fog. No information was available that indicated the possibility of human exposure to such a high concentration of SHC. Consequently, the effects seen in one rat, though biologically significant within 48 h postexposure period, would not be expected to persist or result in long-term health impairment.

Table 8 is a summary of these acute test results with SHC. Under the conditions of these tests, SHC did not demonstrate an acute toxicological hazard.

TABLE 8. SUMMARY OF ACUTE TEST RESULTS FOR SILAHYDROCARBON

Eye Irritation	Skin Irritation	Sensitization	Oral LD_{50} (g/kg)	Dermal LD_{50} (g/kg)	Inhalation LC_{50} (mg/L)
Slight	Negative	Negative	>5.0	>2.0	>4.8

SECTION 6

REFERENCES

Barcikowski, R. S. 1983. Computer Packages and Research Design. Lanham, MD, University Press of America, Vol. 1.

Draize, J. H. 1959. Dermal toxicity, Appraisal of the Safety of Chemicals in Food, Drugs, and Cosmetics. The Staff of the Division of Pharmacology of the Federal Food and Drug Administration. Austin, TX. The Editorial Committee of the Associates of Food and Drug Officials of the United States.

APPENDIX A

DRAIZE[a] SCALE FOR SCORING OCULAR LESIONS

Parameter		Score
1 CORNEA		
A Opacity-degree of density (area most dense taken for reading)		
No opacity		0
Scattered or diffuse areas, details of iris clearly visible		1
Easily discernible translucent areas, details of iris slightly obscured		2
Opalescent areas, no details of iris visible, size of pupil barely discernible		3
Opaque, iris invisible		4
B Area of cornea involved		
One-quarter (or less), but not zero		1
Greater than one-quarter, but less than one-half		2
Greater than one-half, but less than three-quarters		3
Greater than three quarters, up to whole area		4
Score = A x B x 5	Total Maximum =	80
2 IRIS		
A Values		
Normal		0
Folds above normal, congestion, swelling, circumcorneal injection (any or all of these or combination of any thereof) iris still reacting to light (sluggish reaction is positive)		1
No reaction to light, hemorrhage, gross destruction (any or all of these)		2
Score = A x 5	Total Maximum =	10
3 CONJUNCTIVAE		
A Redness (refers to palpebral and bulbar conjunctivae excluding cornea and iris)		
Vessels normal		0
Vessels definitely injected above normal		1
More diffuse, deeper crimson red, individual vessels not easily discernible		2
Diffuse beefy red		3

continued

APPENDIX A (continued)

	Parameter	Score
B	Chemosis	
	No swelling	0
	Any swelling above normal (including nictitating membrane)	1
	Obvious swelling with partial eversion of lids	2
	Swelling with lids about half closed	3
	Swelling with lids above half closed to completely closed	4
C	Discharge	
	No discharge	0
	Any amount different from normal (does not include small amounts observed in inner canthus of normal animals)	1
	Discharge with moistening of the lids and hairs just adjacent to lids	2
	Discharge with moistening of the lids and hairs, and considerable area around the eye	3
Score = (A + B + C) x 2	Total Maximum =	20

The TOTAL MAXIMUM SCORE is the sum of all scores obtained for the cornea, iris, and conjunctivae.

Total Maximum Score Possible =	110

[4] Draize, J.H., G. Woodard, and H.O. Calvery. 1944. Methods for the Study of Irritation and Toxicity of Substances Applied Topically to the Skin and Mucous Membranes. *J. Pharm. Exp. Therap.* 32: 377-390.

APPENDIX B

DRAIZE[a] SCALE FOR EVALUATION AND SCORING OF SKIN REACTIONS

Parameter	Score
1. ERYTHEMA	
No erythema	0
Very slight erythema (barely perceptible)	1
Well-defined erythema	2
Moderate to severe erythema	3
Severe erythema (beet redness)	4
2. EDEMA	
No edema	0
Very slight edema (barely perceptible)	1
Slight edema (edges of area well defined by definited raising)	2
Moderate edema (raising approx 1 mm)	3
Severe edema (raising more than 1 mm and extending beyond area of exposure)	4
3. NECROSIS[b]	
No necrosis	0
Slight necrosis (less than one-fourth exposed area)	5
Moderate necrosis (one-fourth to one-half exposed area)	10
Severe necrosis (more than one-half exposed area)	15

[a] Draize J.H., G. Woodard, and H.O. Calvery. 1944. Methods for the Study of Irritation and Toxicity of Substances Applied Topically to the Skin and Mucous Membranes. *J. Pharm. Exp. Therap.* 32:377-390.

[b] Necrosis, for the purpose of this scoring system, is defined as a chemical denaturation of tissue sufficiently severe to result in fibrotic replacement (scar tissue). Superficial eschar that heals without scar is not classified as necrosis.

APPENDIX C

NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH INTERPRETATION OF SKIN RATINGS[a]

	Rating	Interpretation
Intact Skin	0 – 0.9	Nonirritant; probably safe for human skin contact
	1 – 1.9	Mild irritant; may be safe for use, but appropriate protective measures are recommended during contact
	2 – 4	Too irritating for human skin contact; avoid contact

[a] Campbell, K.H., E.L. George, C.C. Hale, and J.F. Stara. 1975. Dermal Irritancy of Metal Compounds. *Arch. Environ. Health* 30: 168-170.

APPENDIX D

GRADING SYSTEM[a] FOR SENSITIZATION TEST

Erythema			Edema		
0	–	None	0	–	None
1	–	Very Slight Pink	1	–	Very Slight
2	–	Slight Pink	2	–	Slight
3	–	Moderate Red	3	–	Moderate
4	–	Very Red	4	–	Marked

[a] Toxic Hazards Research Unit grading system for sensitization test.

APPENDIX E

SCALE[a] FOR DETERMINING SENSITIZATION POTENTIAL

Sensitization Rate (%)	Grade
10	Weak
20 – 30	Mild
40 – 60	Moderate
70 – 80	Strong
90 – 100	Extreme

[a] Toxic Hazards Research Unit grading system for sensitization potential.

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QUALITY ASSURANCE

The study, "Evaluation of the Acute Toxicity of Silahydrocarbon," was conducted by the NSI Technology Services Corporation, Toxic Hazards Research Unit using the guidance of the Environmental Protection Agency's Good Laboratory Practices Guidelines, 40CFR PART 792. The various phases of this study were inspected by members of the Quality Assurance Unit. Results of these inspections were reported directly to the Study Director at the close of each inspection.

DATE OF INSPECTION:	ITEM INSPECTED:
28FEB89 - 3MAR89	Skin Irritation
6 - 10MAR89	Eye Irritation
27MAR89 - 21APR89	Skin Sensitization
14JUN89 - 10JUL89	Final Report

The Quality Assurance Unit has determined by review process that this report accurately describes those methods and standard operating procedures required by the protocol. The reported results accurately reflect the raw data obtained during the course of the study in most instances. Discrepancies were found in the form of missing data that might substantiate statements presented in this Final Report.

There were significant discrepancies noted during the course of the final report inspection which would preclude general acceptance of this study as having been conducted according to the requirements as outlined in EPA TITLE 40 Part 792.

M. G. Schneider
QA Coordinator
Toxic Hazards Research Unit

Date 10 July 1989